

Docket No. PH-7076-A
Serial No.: 09/505,788

SUPPORT FOR THE AMENDMENTS

It is submitted that the amendments to the Claims are well supported by the disclosure of the application as filed.

Applicants submit that no new matter will be entered upon entry of this amendment.

REMARKS

Reconsideration and re-examination is respectfully requested. The indication of allowable subject matter is acknowledged with appreciation.

After entering these amendments, Claims 1-4, 6, 8, 10-14, 16, 18, 20, 22, 23, 25, 26 and 27-56 will be pending. Claims 1, 10, 20, and 23 have been rewritten. The marked-up version of these amendments is found on a separate sheet attached to this amendment and titled "Marked-Up Version of Rewritten Claims". It is respectfully requested that the amendments above be entered before examination of the application.

Rejection under 35 USC 112, 2nd paragraph.

The Examiner has rejected Claim 10 under 35 USC 112, 2nd paragraph as being indefinite in the definition of R¹¹ for the limitation "=O". Applicants have amended the Claim 10 to deleted the term "=O". In view of the present amendments Applicants submit the rejection is moot.

Rejection under 35 USC 112, 2nd paragraph.

The Examiner has rejected Claim 20 under 35 USC 112, 2nd paragraph as being indefinite in the definition of R²⁰ for the limitation "4-MeS-phenyl)CH₂-". Applicants submit the missing parenthesis is a typographical error and have amended the definition of R²⁰ to read "(4-MeS-phenyl)CH₂-".

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accordingly. In view of the present amendments Applicants submit the rejection is moot.

Rejection under 35 USC 112, 2nd paragraph.

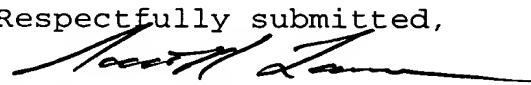
The Examiner has rejected Claim 20 under 35 USC 112, 2nd paragraph as being indefinite in the definition of R¹¹ for the limitation "=O". Applicants have amended the Claim 20 to deleted the term "=O". In view of the present amendments Applicants submit the rejection is moot.

Rejection under 35 USC 112, 2nd paragraph.

The Examiner has rejected Claim 23 under 35 USC 112, 2nd paragraph as being indefinite in the phrase "Alzheimer's Disease production". Applicants have deleted the term "production". In view of the present amendments Applicants submit the rejection is moot.

The application is now believed to be in condition for allowance and an early notification thereof is respectfully requested.

Respectfully submitted,


9/24/02
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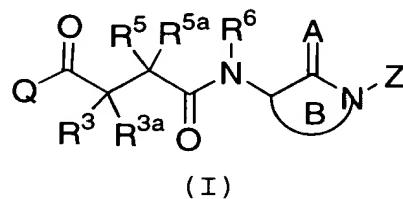
Marked-Up Version of Rewritten Claims

1, 10, 20, and 23.

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1. (Thrice Amended) A compound of Formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

A is O or S;

Q is $-NR^1R^2$;

R^1 is selected from: H and C_1-C_6 alkyl;

R^2 is independently selected from H and C_1-C_6 alkyl;

R^3 is $-(CR^7R^{7a})_n-R^4$,

$-(CR^7R^{7a})_n-S-(CR^7R^{7a})_m-R^4$,

$-(CR^7R^{7a})_n-O-(CR^7R^{7a})_m-R^4$,

$-(CR^7R^{7a})_n-N(R^{7b})-(CR^7R^{7a})_m-R^4$,

$-(CR^7R^{7a})_n-S(=O)-(CR^7R^{7a})_m-R^4$,

$-(CR^7R^{7a})_n-S(=O)_2-(CR^7R^{7a})_m-R^4$,

$-(CR^7R^{7a})_n-C(=O)-(CR^7R^{7a})_m-R^4$,

$-(CR^7R^{7a})_n-N(R^{7b})C(=O)-(CR^7R^{7a})_m-R^4$,

$-(CR^7R^{7a})_n-C(=O)N(R^{7b})-(CR^7R^{7a})_m-R^4$,

$-(CR^7R^{7a})_n-N(R^{7b})S(=O)_2-(CR^7R^{7a})_m-R^4$, or

$-(CR^7R^{7a})_n-S(=O)_2N(R^{7b})-(CR^7R^{7a})_m-R^4$;

n is 0, 1, 2, or 3;

m is 0, 1, 2, or 3;

R^{3a} is H, OH, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₂-C₄ alkenyl or C₂-C₄ alkenyloxy;

R⁴ is H, OH, OR^{14a},
C₁-C₆ alkyl substituted with 0-3 R^{4a},
C₂-C₆ alkenyl substituted with 0-3 R^{4a},
C₂-C₆ alkynyl substituted with 0-3 R^{4a},
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle
is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from
H, F, Cl, Br, I, CF₃,
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle
is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H,
OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃,
S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R⁵ is H, OR¹⁴;

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C₁-C₆ alkyl substituted with 0-3 R^{5b};
C₁-C₆ alkoxy substituted with 0-3 R^{5b};
C₂-C₆ alkenyl substituted with 0-3 R^{5b};
C₂-C₆ alkynyl substituted with 0-3 R^{5b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle
is substituted with 0-3 R^{5c};

R^{5a} is H, OH, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₂-C₄ alkenyl, or
C₂-C₄ alkenyloxy;

R^{5b}, at each occurrence, is independently selected from:
H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂,
NR¹⁵R¹⁶;
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle
is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H,
OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃,
S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R⁶ is H;
C₁-C₆ alkyl substituted with 0-3 R^{6a};
C₃-C₁₀ carbocycle substituted with 0-3 R^{6b}; or
C₆-C₁₀ aryl substituted with 0-3 R^{6b};

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R^{6a} , at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14} , Cl, F, Br, I, $=O$, CN, NO_2 , $NR^{15}R^{16}$, aryl or CF_3 ;

R^{6b} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^7 , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , CF_3 , phenyl and C_1-C_4 alkyl;

R^{7a} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , CF_3 , and C_1-C_4 alkyl;

R^{7b} is independently selected from H and C_1-C_4 alkyl;

Ring B is a 7 membered lactam or thiolactam, wherein the lactam is 2-oxo-azepinyl or thiolactam is 2-thioxo-azepinyl; wherein each additional lactam carbon or thiolactam carbon is substituted with 0-2 R^{11} ; provided two R^{11} substituents are present on adjacent atoms and are combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{13} ;

and,

wherein the lactam or thiolactam contains a heteroatom selected from $-N=$, $-NH-$, and $-N(R^{10})-$;

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$; C_1-C_6 alkyl optionally substituted with 0-3 R^{10a} ; C_6-C_{10} aryl substituted with 0-4 R^{10b} ; C_3-C_{10} carbocycle substituted with 0-3 R^{10b} ; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R¹¹, at each occurrence, is independently selected from H, C₁-C₄ alkoxy, Cl, F, Br, I, [=O,] CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃; C₁-C₆ alkyl optionally substituted with 0-3 R^{11a}; C₆-C₁₀ aryl substituted with 0-3 R^{11b}; C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃; phenyl substituted with 0-3 R^{11b}; C₃-C₆ cycloalkyl substituted with 0-3 R^{11b}; and 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11b} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , acetyl, SCH_3 , $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

Z is H;

C_1-C_8 alkyl substituted with 1-3 R^{12} ;
 C_2-C_4 alkenyl substituted with 1-3 R^{12} ;
 C_2-C_4 alkynyl substituted with 1-3 R^{12} ;
 C_1-C_8 alkyl substituted with 0-3 R^{12a} ;
 C_2-C_4 alkenyl substituted with 0-3 R^{12a} ;
 C_2-C_4 alkynyl substituted with 0-3 R^{12a} ;
 C_6-C_{10} aryl substituted with 0-4 R^{12b} ;
 C_3-C_{10} carbocycle substituted with 0-4 R^{12b} ; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b} ;

R^{12} , at each occurrence, is independently selected from C_6-C_{10} aryl substituted with 0-4 R^{12b} ;
 C_3-C_{10} carbocycle substituted with 0-4 R^{12b} ; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b} ;

R^{12a} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , $-C(=O)NR^{15}R^{16}$, CF_3 , acetyl, SCH_3 , $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, or C_1-C_4 haloalkyl-S-;

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R^{12b} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , acetyl, SCH_3 , $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13} , at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, and CF_3 ;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15} , at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, $(C_1-C_6$ alkyl)-C(=O)-, and $(C_1-C_6$ alkyl)-S(=O)₂-;

R^{16} , at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, $(C_1-C_6$ alkyl)-C(=O)-, and $(C_1-C_6$ alkyl)-S(=O)₂-;

R^{17} is H, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, aryl substituted by 0-4 R^{17a} , or - CH_2 -aryl substituted by 0-4 R^{17a} ;

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF_3 , OCF_3 , SCH_3 , $S(O)CH_3$, SO_2CH_3 , - NH_2 , - $N(CH_3)_2$, or C_1-C_4 haloalkyl;

R^{18} , at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, $(C_1-C_6$ alkyl)-C(=O)-, and $(C_1-C_6$ alkyl)-S(=O)₂-; and

R^{19} , at each occurrence, is independently selected from H, OH, C_1 - C_6 alkyl, phenyl, benzyl, phenethyl, $(C_1$ - C_6 alkyl)- $C(=O)$ -, and $(C_1$ - C_6 alkyl)- $S(=O)_2$ -;

provided, when R^{13} is H,

then Z is H;

C_4 - C_8 alkyl substituted with 1-3 R^{12} ;

C_2 - C_4 alkenyl substituted with 1-3 R^{12} ;

C_2 - C_4 alkynyl substituted with 1-3 R^{12} ;

C_1 - C_8 alkyl substituted with 0-3 R^{12a} ;

C_2 - C_4 alkenyl substituted with 0-3 R^{12a} ; or

C_2 - C_4 alkynyl substituted with 0-3 R^{12a} ; and

provided, when ring B is a 1,3,4,5-tetrahydro-1-(Z)-5- (R^{10}) -6,6,7,7-tetra(R^{11})-2,4-dioxo-2H-1,5-diazepin-3-yl core, and R^{13} is H; then

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$,

$S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$; or

C_1 - C_6 alkyl optionally substituted with 0-3 R^{10a} ;

R^{10a} , at each occurrence, is independently selected from H, C_1 - C_6 alkyl, OR^{14} , Cl, F, Br, I, $=O$, CN, NO_2 , $NR^{15}R^{16}$, and CF_3 .

10. (Thrice Amended) A compound, according to one of Claims 6, 8, or 25 wherein:

R^3 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_3$, $-CH(CH_3)_2$, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CF_3$, $-CH_2CH_2CF_3$, $-CH_2CH_2CH_2CF_3$, $-CH=CH_2$, $-CH_2CH=CH_2$, $-CH_2C(CH_3)=CH_2$, $-CH_2CH_2CH=CH_2$, $cis-CH_2CH=CH(CH_3)$, $trans-CH_2CH=CH(CH_3)$,

$-\text{C}\equiv\text{CH}$, $-\text{CH}_2\text{C}\equiv\text{CH}$, $-\text{CH}_2\text{C}\equiv\text{C}(\text{CH}_3)$,
 cyclopropyl-CH_2- , cyclobutyl-CH_2- , cyclopentyl-CH_2- ,
 cyclohexyl-CH_2- , $\text{cyclopropyl-CH}_2\text{CH}_2-$,
 $\text{cyclobutyl-CH}_2\text{CH}_2-$, $\text{cyclopentyl-CH}_2\text{CH}_2-$,
 $\text{cyclohexyl-CH}_2\text{CH}_2-$, phenyl-CH_2- ,
 $(2\text{-F-phenyl})\text{CH}_2-$, $(3\text{-F-phenyl})\text{CH}_2-$, $(4\text{-F-phenyl})\text{CH}_2-$,
 $(2\text{-Cl-phenyl})\text{CH}_2-$, $(3\text{-Cl-phenyl})\text{CH}_2-$, $(4\text{-Cl-phenyl})\text{CH}_2-$,
 $(2,3\text{-diF-phenyl})\text{CH}_2-$, $(2,4\text{-diF-phenyl})\text{CH}_2-$,
 $(2,5\text{-diF-phenyl})\text{CH}_2-$, $(2,6\text{-diF-phenyl})\text{CH}_2-$,
 $(3,4\text{-diF-phenyl})\text{CH}_2-$, $(3,5\text{-diF-phenyl})\text{CH}_2-$,
 $(2,3\text{-diCl-phenyl})\text{CH}_2-$, $(2,4\text{-diCl-phenyl})\text{CH}_2-$,
 $(2,5\text{-diCl-phenyl})\text{CH}_2-$, $(2,6\text{-diCl-phenyl})\text{CH}_2-$,
 $(3,4\text{-diCl-phenyl})\text{CH}_2-$, $(3,5\text{-diCl-phenyl})\text{CH}_2-$,
 $(3\text{-F-4-Cl-phenyl})\text{CH}_2-$, $(3\text{-F-5-Cl-phenyl})\text{CH}_2-$,
 $(3\text{-Cl-4-F-phenyl})\text{CH}_2-$, $\text{phenyl-CH}_2\text{CH}_2-$,
 $(2\text{-F-phenyl})\text{CH}_2\text{CH}_2-$, $(3\text{-F-phenyl})\text{CH}_2\text{CH}_2-$,
 $(4\text{-F-phenyl})\text{CH}_2\text{CH}_2-$, $(2\text{-Cl-phenyl})\text{CH}_2\text{CH}_2-$,
 $(3\text{-Cl-phenyl})\text{CH}_2\text{CH}_2-$, $(4\text{-Cl-phenyl})\text{CH}_2\text{CH}_2-$,
 $(2,3\text{-diF-phenyl})\text{CH}_2\text{CH}_2-$, $(2,4\text{-diF-phenyl})\text{CH}_2\text{CH}_2-$,
 $(2,5\text{-diF-phenyl})\text{CH}_2\text{CH}_2-$, $(2,6\text{-diF-phenyl})\text{CH}_2\text{CH}_2-$,
 $(3,4\text{-diF-phenyl})\text{CH}_2\text{CH}_2-$, $(3,5\text{-diF-phenyl})\text{CH}_2\text{CH}_2-$,
 $(2,3\text{-diCl-phenyl})\text{CH}_2\text{CH}_2-$, $(2,4\text{-diCl-phenyl})\text{CH}_2\text{CH}_2-$,
 $(2,5\text{-diCl-phenyl})\text{CH}_2\text{CH}_2-$, $(2,6\text{-diCl-phenyl})\text{CH}_2\text{CH}_2-$,
 $(3,4\text{-diCl-phenyl})\text{CH}_2\text{CH}_2-$, $(3,5\text{-diCl-phenyl})\text{CH}_2\text{CH}_2-$,
 $(3\text{-F-4-Cl-phenyl})\text{CH}_2\text{CH}_2-$, or $(3\text{-F-5-Cl-phenyl})\text{CH}_2\text{CH}_2-$,

R^5 is $-\text{CH}_3$, $-\text{CH}_2\text{CH}_3$, $-\text{CH}_2\text{CH}_2\text{CH}_3$, $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$,
 $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$, $-\text{CH}_2\text{CH}(\text{CH}_3)_2$, $-\text{CH}_2\text{C}(\text{CH}_3)_3$,
 $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_3$, $-\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$,
 $-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$, $-\text{CH}(\text{CH}_2\text{CH}_3)_2$, $-\text{CH}_2\text{CF}_3$, $-\text{CH}_2\text{CH}_2\text{CF}_3$,
 $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CF}_3$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CF}_3$, $-\text{CH}=\text{CH}_2$, $-\text{CH}_2\text{CH}=\text{CH}_2$,
 $-\text{CH}=\text{CHCH}_3$, $\text{cis-CH}_2\text{CH}=\text{CH}(\text{CH}_3)$, $\text{trans-CH}_2\text{CH}=\text{CH}(\text{CH}_3)$,
 $\text{trans-CH}_2\text{CH}=\text{CH}(\text{C}_6\text{H}_5)$, $-\text{CH}_2\text{CH}=\text{C}(\text{CH}_3)_2$, $\text{cis-CH}_2\text{CH}=\text{CHCH}_2\text{CH}_3$,
 $\text{trans-CH}_2\text{CH}=\text{CHCH}_2\text{CH}_3$, $\text{cis-CH}_2\text{CH}_2\text{CH}=\text{CH}(\text{CH}_3)$,

trans-CH₂CH₂CH=CH(CH₃), *trans*-CH₂CH=CHCH₂(C₆H₅),
-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), -CH₂C≡C(C₆H₅),
-CH₂CH₂C≡CH, -CH₂CH₂C≡C(CH₃), -CH₂CH₂C≡C(C₆H₅),
cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-,
cyclohexyl-CH₂-, (2-CH₃-cyclopropyl)CH₂-,
(3-CH₃-cyclobutyl)CH₂-,
cyclopropyl-CH₂CH₂-, cyclobutyl-CH₂CH₂-,
cyclopentyl-CH₂CH₂-, cyclohexyl-CH₂CH₂-,
(2-CH₃-cyclopropyl)CH₂CH₂-, (3-CH₃-cyclobutyl)CH₂CH₂-,
phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
(4-F-phenyl)CH₂-, furanyl-CH₂-, thienyl-CH₂-,
pyridyl-CH₂-, 1-imidazolyl-CH₂-, oxazolyl-CH₂-,
isoxazolyl-CH₂-,
phenyl-CH₂CH₂-, (2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
(4-F-phenyl)CH₂CH₂-, furanyl-CH₂CH₂-, thienyl-CH₂CH₂-,
pyridyl-CH₂CH₂-, 1-imidazolyl-CH₂CH₂-, oxazolyl-CH₂CH₂-,
isoxazolyl-CH₂CH₂-;

Z is methyl, ethyl, i-propyl, n-propyl, n-butyl, i-butyl,
s-butyl, t-butyl, or allyl;

R¹⁰ is H, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, or
(4-CF₃-phenyl)CH₂CH₂-;

R¹¹, at each occurrence, is independently selected from
H, [=O,] methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
3-F-phenyl, (3-F-phenyl)CH₂-, (3-F-phenyl)CH₂CH₂-,
2-F-phenyl, (2-F-phenyl)CH₂-, (2-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
3-Cl-phenyl, (3-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂CH₂-,

4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
3-CH₃-phenyl, (3-CH₃-phenyl)CH₂-, (3-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, (4-CF₃-phenyl)CH₂CH₂-,
pyrid-2-yl, pyrid-3-yl, or pyrid-4-yl, and

R¹³, at each occurrence, is independently selected from
H, F, Cl, OH, -CH₃, -CH₂CH₃, -OCH₃, or -CF₃.

20. (Thrice Amended) A compound according to one of Claims
16, 18, or 26 wherein:

R³ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH₂CH₂CH₂CH₃,
-CH(CH₃)₂, -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂,
-CH₂CF₃, -CH₂CH₂CF₃, -CH₂CH₂CH₂CF₃,
-CH=CH₂, -CH₂CH=CH₂, -CH₂C(CH₃)=CH₂,
-CH₂CH₂CH=CH₂,
cis-CH₂CH=CH(CH₃),
trans-CH₂CH=CH(CH₃),
-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃),
cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-,
cyclohexyl-CH₂-, cyclopropyl-CH₂CH₂-,
cyclobutyl-CH₂CH₂-, cyclopentyl-CH₂CH₂-,
cyclohexyl-CH₂CH₂-, phenyl-CH₂-,
(2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-, (4-F-phenyl)CH₂-,
(2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂-,
(2,3-diF-phenyl)CH₂-, (2,4-diF-phenyl)CH₂-,
(2,5-diF-phenyl)CH₂-, (2,6-diF-phenyl)CH₂-,
(3,4-diF-phenyl)CH₂-, (3,5-diF-phenyl)CH₂-,
(2,3-diCl-phenyl)CH₂-, (2,4-diCl-phenyl)CH₂-,
(2,5-diCl-phenyl)CH₂-, (2,6-diCl-phenyl)CH₂-,
(3,4-diCl-phenyl)CH₂-, (3,5-diCl-phenyl)CH₂-,
(3-F-4-Cl-phenyl)CH₂-, (3-F-5-Cl-phenyl)CH₂-,
(3-Cl-4-F-phenyl)CH₂-, phenyl-CH₂CH₂-,
(2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,

(4-F-phenyl)CH₂CH₂- , (2-Cl-phenyl)CH₂CH₂- ,
(3-Cl-phenyl)CH₂CH₂- , (4-Cl-phenyl)CH₂CH₂- ,
(2,3-diF-phenyl)CH₂CH₂- , (2,4-diF-phenyl)CH₂CH₂- ,
(2,5-diF-phenyl)CH₂CH₂- , (2,6-diF-phenyl)CH₂CH₂- ,
(3,4-diF-phenyl)CH₂CH₂- , (3,5-diF-phenyl)CH₂CH₂- ,
(2,3-diCl-phenyl)CH₂CH₂- , (2,4-diCl-phenyl)CH₂CH₂- ,
(2,5-diCl-phenyl)CH₂CH₂- , (2,6-diCl-phenyl)CH₂CH₂- ,
(3,4-diCl-phenyl)CH₂CH₂- , (3,5-diCl-phenyl)CH₂CH₂- ,
(3-F-4-Cl-phenyl)CH₂CH₂- , or (3-F-5-Cl-phenyl)CH₂CH₂- ,

R⁵ is -CH₃ , -CH₂CH₃ , -CH₂CH₂CH₃ , -CH(CH₃)₂ , -CH₂CH₂CH₂CH₃ ,
-CH(CH₃)CH₂CH₃ , -CH₂CH(CH₃)₂ , -CH₂C(CH₃)₃ ,
-CH₂CH₂CH₂CH₂CH₃ , -CH(CH₃)CH₂CH₂CH₃ , -CH₂CH(CH₃)CH₂CH₃ ,
-CH₂CH₂CH(CH₃)₂ , -CH(CH₂CH₃)₂ , -CH₂CF₃ , -CH₂CH₂CF₃ ,
-CH₂CH₂CH₂CF₃ , -CH₂CH₂CH₂CH₂CF₃ , -CH=CH₂ , -CH₂CH=CH₂ ,
-CH=CHCH₃ , cis-CH₂CH=CH(CH₃) , trans-CH₂CH=CH(CH₃) ,
trans-CH₂CH=CH(C₆H₅) , -CH₂CH=C(CH₃)₂ , cis-CH₂CH=CHCH₂CH₃ ,
trans-CH₂CH=CHCH₂CH₃ , cis-CH₂CH₂CH=CH(CH₃) ,
trans-CH₂CH₂CH=CH(CH₃) , trans-CH₂CH=CHCH₂(C₆H₅) ,
-C≡CH , -CH₂C≡CH , -CH₂C≡C(CH₃) , -CH₂C≡C(C₆H₅) ,
-CH₂CH₂C≡CH , -CH₂CH₂C≡C(CH₃) , -CH₂CH₂C≡C(C₆H₅) ,
cyclopropyl-CH₂- , cyclobutyl-CH₂- , cyclopentyl-CH₂- ,
cyclohexyl-CH₂- , (2-CH₃-cyclopropyl)CH₂- ,
(3-CH₃-cyclobutyl)CH₂- ,
cyclopropyl-CH₂CH₂- , cyclobutyl-CH₂CH₂- ,
cyclopentyl-CH₂CH₂- , cyclohexyl-CH₂CH₂- ,
(2-CH₃-cyclopropyl)CH₂CH₂- , (3-CH₃-cyclobutyl)CH₂CH₂- ,
phenyl-CH₂- , (2-F-phenyl)CH₂- , (3-F-phenyl)CH₂- ,
(4-F-phenyl)CH₂- , furanyl-CH₂- , thieryl-CH₂- ,
pyridyl-CH₂- , 1-imidazolyl-CH₂- , oxazolyl-CH₂- ,
isoxazolyl-CH₂- ,
phenyl-CH₂CH₂- , (2-F-phenyl)CH₂CH₂- , (3-F-phenyl)CH₂CH₂- ,
(4-F-phenyl)CH₂CH₂- , furanyl-CH₂CH₂- , thieryl-CH₂CH₂- ,
pyridyl-CH₂CH₂- , 1-imidazolyl-CH₂CH₂- , oxazolyl-CH₂CH₂- ,
isoxazolyl-CH₂CH₂- ;

Z is phenyl, 2-F-phenyl, 3-F-phenyl, 4-F-phenyl,
2-Cl-phenyl, 3-Cl-phenyl, 4-Cl-phenyl, 2,3-diF-phenyl,
2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl,
3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl,
2,4-diCl-phenyl, 2,5-diCl-phenyl, 2,6-diCl-phenyl,
3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl,
3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl,
3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl,
4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl,
2-CF₃O-phenyl, 3-CF₃O-phenyl, 4-CF₃O-phenyl,
furanyl, thienyl, pyridyl, 2-Me-pyridyl, 3-Me-pyridyl,
4-Me-pyridyl, 1-imidazolyl, oxazolyl, isoxazolyl,
cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl,
N-piperidinyl,
phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
(4-F-phenyl)CH₂-, (2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-,
(4-Cl-phenyl)CH₂-, (2,3-diF-phenyl)CH₂-,
(2,4-diF-phenyl)CH₂-, (2,5-diF-phenyl)CH₂-,
(2,6-diF-phenyl)CH₂-, (3,4-diF-phenyl)CH₂-,
(3,5-diF-phenyl)CH₂-, (2,3-diCl-phenyl)CH₂-,
(2,4-diCl-phenyl)CH₂-, (2,5-diCl-phenyl)CH₂-,
(2,6-diCl-phenyl)CH₂-, (3,4-diCl-phenyl)CH₂-,
(3,5-diCl-phenyl)CH₂-, (3-F-4-Cl-phenyl)CH₂-,
(3-F-5-Cl-phenyl)CH₂-, (3-Cl-4-F-phenyl)CH₂-,
(2-MeO-phenyl)CH₂-, (3-MeO-phenyl)CH₂-,
(4-MeO-phenyl)CH₂-, (2-Me-phenyl)CH₂-,
(3-Me-phenyl)CH₂-, (4-Me-phenyl)CH₂-,
(2-MeS-phenyl)CH₂-, (3-MeS-phenyl)CH₂-,
(4-MeS-phenyl)CH₂-, (2-CF₃O-phenyl)CH₂-,
(3-CF₃O-phenyl)CH₂-, (4-CF₃O-phenyl)CH₂-,
(furanyl)CH₂-, (thienyl)CH₂-, (pyridyl)CH₂-,
(2-Me-pyridyl)CH₂-, (3-Me-pyridyl)CH₂-,
(4-Me-pyridyl)CH₂-, (1-imidazolyl)CH₂-,
(oxazolyl)CH₂-, (isoxazolyl)CH₂-,

(cyclopropyl)CH₂-, (cyclobutyl)CH₂-, (cyclopentyl)CH₂-,
(cyclohexyl)CH₂-, (N-piperidinyl)CH₂-,

phenyl-CH₂CH₂-, (phenyl)CH₂CH₂-, (2-F-phenyl)CH₂CH₂-,
(3-F-phenyl)CH₂CH₂-, (4-F-phenyl)CH₂CH₂-,
(2-Cl-phenyl)CH₂CH₂-, (3-Cl-phenyl)CH₂CH₂-,
(4-Cl-phenyl)CH₂CH₂-, (2,3-diF-phenyl)CH₂CH₂-,
(2,4-diF-phenyl)CH₂CH₂-, (2,5-diF-phenyl)CH₂CH₂-,
(2,6-diF-phenyl)CH₂CH₂-, (3,4-diF-phenyl)CH₂CH₂-,
(3,5-diF-phenyl)CH₂CH₂-, (2,3-diCl-phenyl)CH₂CH₂-,
(2,4-diCl-phenyl)CH₂CH₂-, (2,5-diCl-phenyl)CH₂CH₂-,
(2,6-diCl-phenyl)CH₂CH₂-, (3,4-diCl-phenyl)CH₂CH₂-,
(3,5-diCl-phenyl)CH₂CH₂-, (3-F-4-Cl-phenyl)CH₂CH₂-,
(3-F-5-Cl-phenyl)CH₂CH₂-, (3-Cl-4-F-phenyl)CH₂CH₂-,
(2-MeO-phenyl)CH₂CH₂-, (3-MeO-phenyl)CH₂CH₂-,
(4-MeO-phenyl)CH₂CH₂-, (2-Me-phenyl)CH₂CH₂-,
(3-Me-phenyl)CH₂CH₂-, (4-Me-phenyl)CH₂CH₂-,
(2-MeS-phenyl)CH₂CH₂-, (3-MeS-phenyl)CH₂CH₂-,
(4-MeS-phenyl)CH₂CH₂-, (2-CF₃O-phenyl)CH₂CH₂-,
(3-CF₃O-phenyl)CH₂CH₂-, (4-CF₃O-phenyl)CH₂CH₂-,
(furanyl)CH₂CH₂-, (thienyl)CH₂CH₂-, (pyridyl)CH₂CH₂-,
(2-Me-pyridyl)CH₂CH₂-, (3-Me-pyridyl)CH₂CH₂-,
(4-Me-pyridyl)CH₂CH₂-, (imidazolyl)CH₂CH₂-,
(oxazolyl)CH₂CH₂-, (isoxazolyl)CH₂CH₂-,
(cyclopropyl)CH₂CH₂-, (cyclobutyl)CH₂CH₂-,
(cyclopentyl)CH₂CH₂-, (cyclohexyl)CH₂CH₂-, or
(N-piperidinyl)CH₂CH₂-;

R¹⁰ is H, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, or
(4-CF₃-phenyl)CH₂CH₂-;

R^{11} , at each occurrence, is independently selected from H, [=O,] methyl, ethyl, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-, 3-F-phenyl, (3-F-phenyl)CH₂-, (3-F-phenyl)CH₂CH₂-, 2-F-phenyl, (2-F-phenyl)CH₂-, (2-F-phenyl)CH₂CH₂-, 4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-, 3-Cl-phenyl, (3-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂CH₂-, 4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-, 3-CH₃-phenyl, (3-CH₃-phenyl)CH₂-, (3-CH₃-phenyl)CH₂CH₂-, 4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, (4-CF₃-phenyl)CH₂CH₂-, pyrid-2-yl, pyrid-3-yl, or pyrid-4-yl, and

R^{13} , at each occurrence, is independently selected from H, F, Cl, OH, -CH₃, -CH₂CH₃, -OCH₃, or -CF₃.

23. (Twice Amended) A method for the treatment of Alzheimer's Disease **[production]** comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 1.